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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,525	KOO ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 24-34* is/are rejected.

7)☒ Claim(s) *8 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 1-10, 24-34 in the reply filed on 7/10/2006 is acknowledged. The species election directed to claim 8 and 31 has been withdrawn upon further consideration.

2. Claims 11-23 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/10/2006.

A first action on the merits of claims 1-10 and 24-34 follows.

Specification

3. The disclosure is objected to because of the following informalities:

The specification recites, " See Su et al, US Ser. No.____, filed December 29, 2003 entitled "Composite Organic-Inorganic Nanoparticles" on page 33, last 2 lines of paragraph 0095). This is the improper citation of a co-pending application.

Appropriate correction is required.

Claim Objections

4. Claims 8 and 31 are objected to because of the following informalities:

The claim refers to tables. MPEP 2173.05(s) states:

Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience."

This rejection may be easily be overcome by amending claims 8 and 31 to recite the labels claimed.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 4 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites, "wherein the nucleotide occurrence of each nucleotide position of a labeled oligonucleotide probe is identified by a number of copies of a unique signal molecule." It is unclear if each nucleotide has a label or there are multiple labels for each nucleotide. It is unclear if the claim is directed to the occurrence of a nucleotide at each position or the occurrence of each nucleotide. It is further unclear if the number of copies of each signal is correspondent to each nucleotide or if each nucleotide has one signal.

Claim 27 recites, "wherein the nucleotide occurrence of each nucleotide position of a labeled oligonucleotide probe is identified by a number of copies of a unique signal molecule." It is unclear if each nucleotide has a label or there are multiple labels for each nucleotide. It is unclear if the claim is directed to the occurrence of a nucleotide at each position or the occurrence of each nucleotide. It is further unclear if the number of

copies of each signal is correspondent to each nucleotide or if each nucleotide has one signal.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 and 24-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are directed to a population of oligonucleotide probes. Oligonucleotide probes are DNA and applicant teaches in table 1, page 11, adenine is a label. Thus the claim read on DNA labeled with adenine, which is cellular DNA. The claims are not directed to an isolated population of labeled oligonucleotide probes such that the claims would be directed to statutory subject matter. This rejection may be easily overcome by amending the claims to recite an "isolated population of labeled oligonucleotide probes" such that it is clear that the "hand of man" is required and the product is nonnaturally occurring.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (Principles of Genetics, Eighth edition, 1991, page 73).

This rejection is drawn to the broad interpretation a population of labeled nucleotides can be the nucleic acids in a cell.

With regards to claim 1, Gardner et al teach a chromosome smear of a man and woman in figure 4.3 A and B. The chromosome came from the cells of a man and a woman. Each chromosome is a population a labeled nucleotide probes associated with a series of detectably distinguishable signal molecules (nucleotides). The 23 chromosomes or probes exceed the number of labeling molecules (adenine, guanine, cytosine and thymidine).

With regards to claim 24, Gardner et al teach a chromosome smear of a man and woman in figure 4.3 A and B. The chromosome came from the cells of a man and a woman. Each chromosome is a population a labeled nucleotide probes associated with a series of detectably distinguishable signal molecules (nucleotides). The 23 chromosomes or probes exceed the number of labeling molecules (adenine, guanine, cytosine and thymidine). Each chromosome is made of double stranded DNA. Thus either strand could be broadly interpreted to be a target polynucleotide and the opposite strand the probe.

10. Claim 1, 2, 5, 7-9, 25, 28, 31, 32, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronin et al (US patent 6,045,996, issued April 4, 2000).

With regards to claim 1, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines

23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine dyes (see column 6, lines 12-22). Cronin further allowing hybridization and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than the number of probes.

With regards to claim 2, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present once, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 5, Cronin teaches fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 7 and 8, Cronin teaches the use of polymethine dyes, fluorescien, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 9, Cronin et al teaches the fluorescien, rhodamine, CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

With regards to claim 24, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines 23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine dyes (see column 6, lines 12-22). Cronin further allowing hybridization of the capture probe and target nucleotide and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than the number of probes.

With regards to claim 25, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present one, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 28, Cronin teaches the fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 31 and 32, Cronin teaches the use of polymethine dyes, fluorescien, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 33, Cronin et al teaches the fluorescien, rhodamine CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

11. Claim 1,2, 5-10, 24, 25, 28-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Han et al (Nature Biotechnology (2001) volume 19, pages 631-635).

Han et al teaches a method of using multicolor optical coding for biological assays. Han teaches the use of 6 colors and 10 intensities could code for 1 million nucleic acid sequences (see abstract).

With regards to claim 1, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence.

With regards to claim 2, Han teaches in figure 5, the use of each label only once.

With regards to claim 5, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5).

With regards to claim 6, Han teaches probes of the same length, namely 14 nucleotides, in figure 5 which are from 10 to 50 nucleotides.

With regards to claim 7 and 8, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 8 depends from claim 7, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1.

With regards to claim 9, Han et al teaches the use of quantum dots (see abstract).

With regards to claim 10, Han teaches the use of quantum dots, which are "zinc sulfide-capped cadmium selenide nanocrystals" (see abstract 2nd line). Han thus teaches the use of nanotags.

With regards to claim 24, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence. Han further teaches the labeled probes are hybridized to the to a complementary strand and are thus a reaction mixture.

With regards to claim 25, Han teaches in figure 5, the use of each label only once. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is present once.

With regards to claim 28, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule has an intensity reference signal.

With regards to claim 29 and 30, Han teaches probes of the same length in figure 5 and are from 10 to 50 nucleotides. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each oligonucleotide is identical in length (claims 29 and 30) and length of 10 to 50 nucleotides.

With regards to claim 31 and 32, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 32 depends from claim 31, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a Raman label or signal molecule from table 1.

With regards to claim 33, Han et al teaches the use of quantum dots (see abstract). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a quantum dot.

With regards to claim 34, Han teaches the use of quantum dots, which are "zinc sulfide-capped cadmium selenide nanocrystals" (see abstract 2nd line). Han thus teaches the use of nanotags.

Summary

No claims are allowed. Claims 3 and 26 appear to be free of the prior art. Claims 3 and 26 are drawn to a population of labeled oligonucleotide probes with unique signals present up to four times per labeled probe. The labeled oligonucleotide probes further comprise a number of unique signal molecules is equal to the number of nucleotides. The closest prior art appears to the concept of labeling each nucleotide

with a unique detectable label appears to be Akhavan-Tafti (US Patent 6,020,138, Issued Feb 1, 2000), which teaches in figure 6 the labeling of small oligonucleotides with different labels. However, Akhavan-Tafti does not teach labeling of each nucleotide with a unique signal molecule and the number of nucleotides equals the number of unique signal molecules.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

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4/26/07